

Supporting Information

A Double Payload Complex between Hypericin and All-*trans* Retinoic Acid in the β -Lactoglobulin Protein

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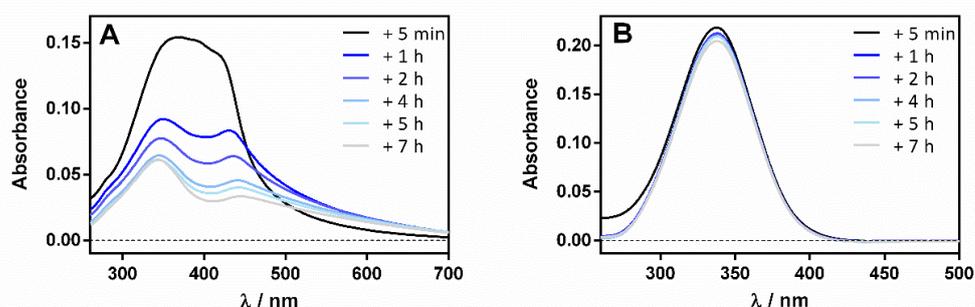


Figure S1. Time evolution of the absorption spectrum of 1.7 μM RA in A) water and B) EtOH.

Citation: Rodríguez-Amigo, B.; Hally, C.; Roig-Yanovsky, N.; Delcanale, P.; Abbruzzetti, S.; Agut, M.; Viappiani, C.; Nonell, S. A Double Payload Complex between Hypericin and All-*trans* Retinoic Acid in the β -Lactoglobulin Protein. *Antibiotics* **2022**, *11*, 282. <https://doi.org/10.3390/antibiotics11020282>

Academic Editor: Marina DellaGreca

Received: 31 December 2021

Accepted: 17 February 2022

Published: 21 February 2022

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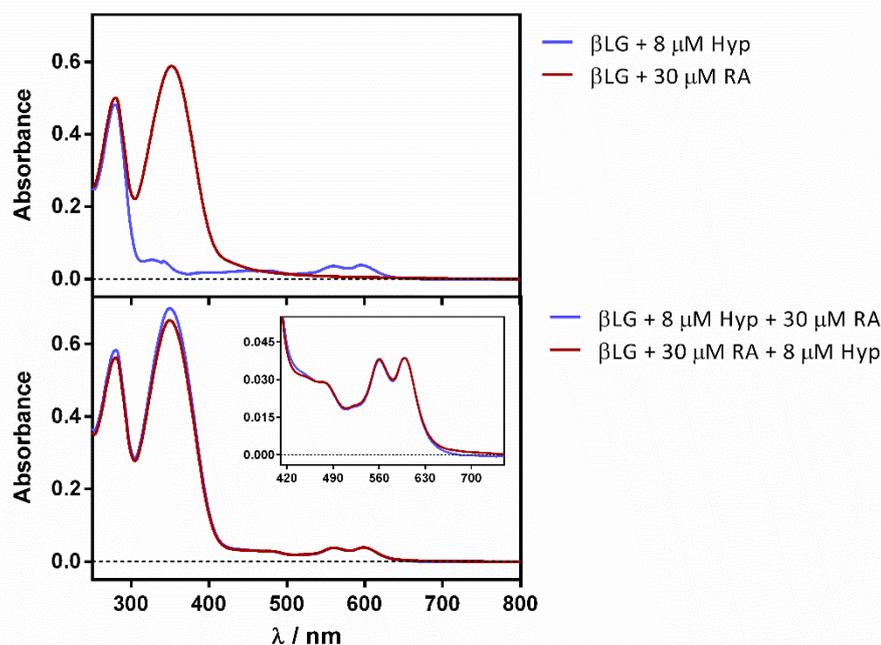


Figure S2. Absorption spectra of Hyp-RA- β LG mixtures, obtained after adding the components in

different order. 30 μM of RA (blue line) were added upon 60 μM of βLG and 8 μM of Hyp, and vice versa.

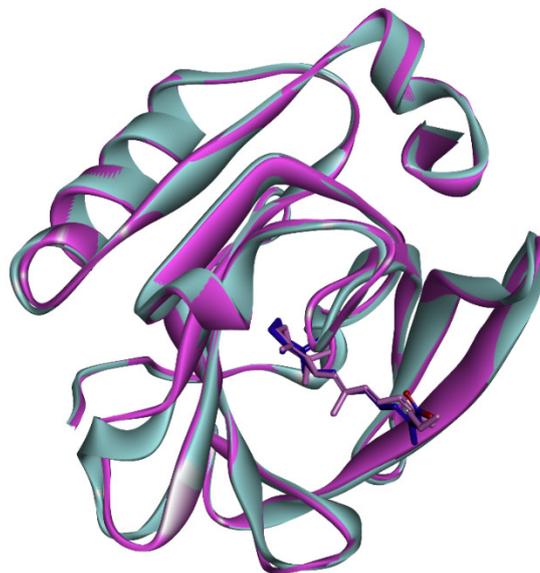


Figure S3. Crystal structures of the complex between retinoic acid and β -lactoglobulin (PDB 1GX9) and between retinol and β -lactoglobulin (PDB 1GX8). For 1GX9, the protein structure is represented as light blue solid ribbon, retinoic acid is represented as blue sticks. For 1GX8, the protein structure is represented as magenta solid ribbon, retinol is represented as magenta sticks.

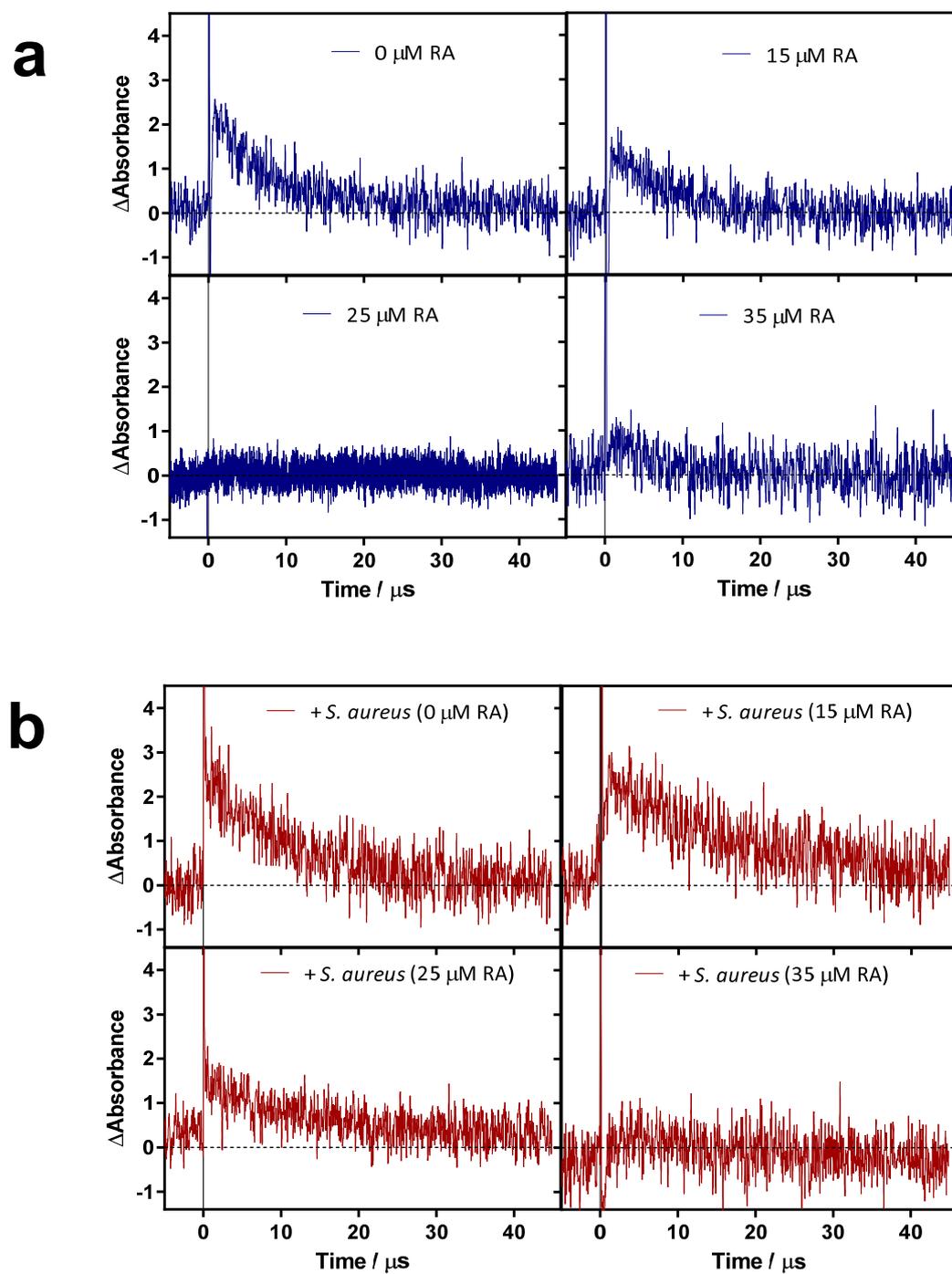


Figure S4. Triplet absorption decay of Hyp-βLG complexes in the absence (a) and presence (b) of *S. aureus*. Solutions containing 60 μM βLG and 15 μM Hyp and different RA concentrations were incubated with *S. aureus* cells for 30 minutes. Transients were acquired at 520 nm after pulsed-laser excitation at 532 nm averaging 100 shots.

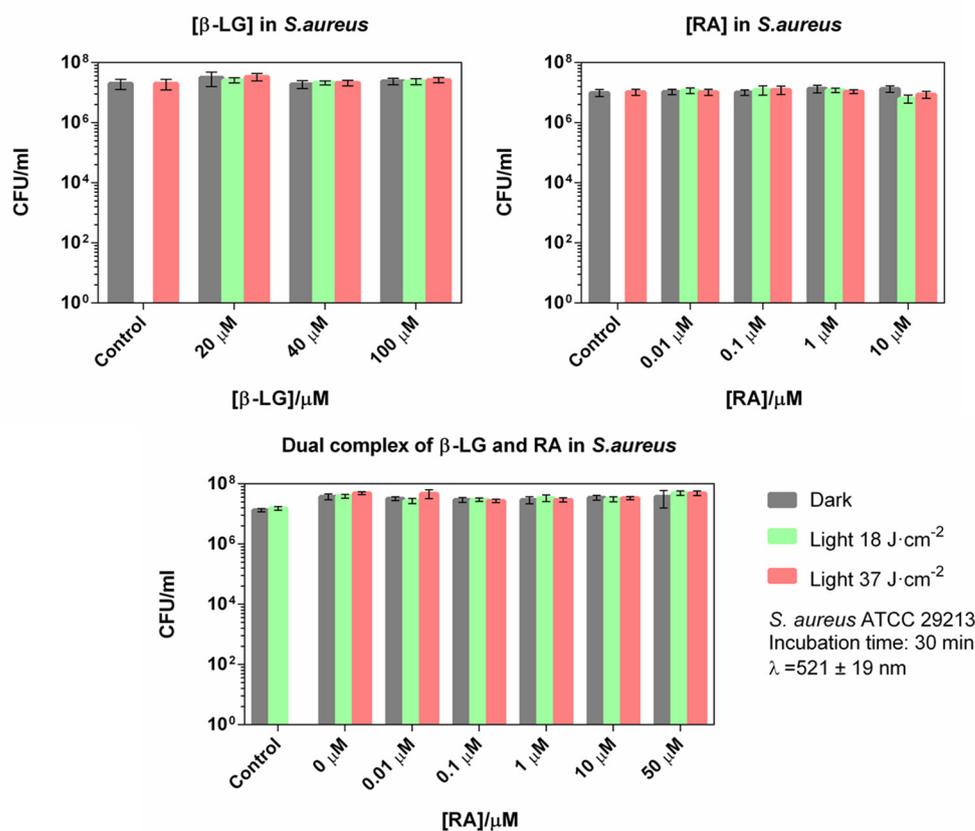


Figure S5. Photoinactivation of *S. aureus* with βLG (Top left), retinoic Acid (Top Right) and the dual complex βLG-RA (Bottom) using green light.

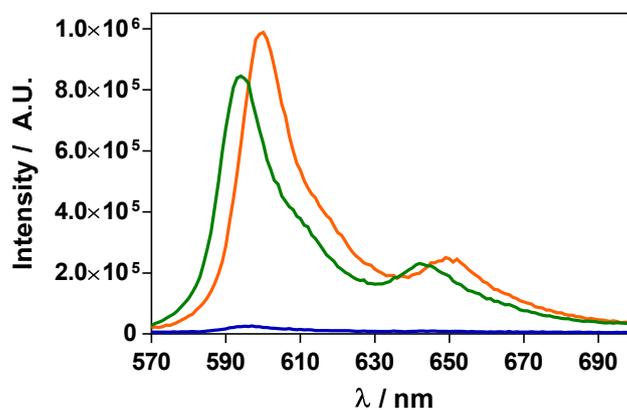


Figure S6. Fluorescence spectra of *S. aureus* incubated with the ternary complex βLG-RA-Hyp immediately after incubation without washing the supernatant (green), resuspending the pellet in PBS after the first centrifugation (blue) and the final pellet resuspended in DMSO after centrifugation (orange). Samples were excited at 550 nm.

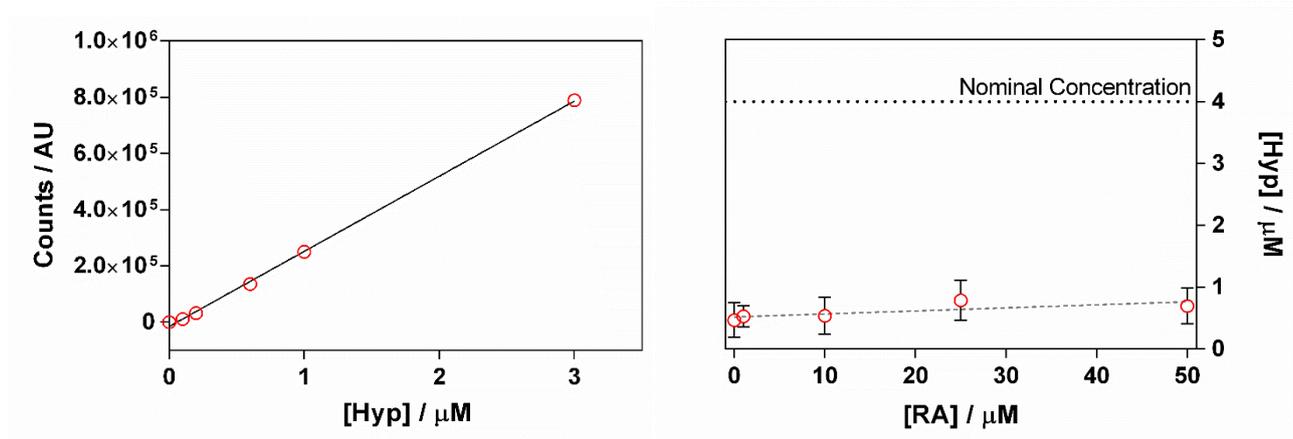


Figure S7. Uptake of hypericin by *S. aureus*, quantified by spectrofluorimetry (left), as a function of retinoic acid concentration (right).